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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,835	07/14/2003	Thomas F. Meyer	0147-0250P	8238

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 09/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/617,835	MEYER ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/043,302.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 12/22/04 has been acknowledged.

Claims 1-9 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well-established utility.

The instant claims are drawn to an isolated nucleic acid sequence and/or any variant thereof that encodes a lipoprotein or any fragment thereof that mediates adhesion of Neisseria cells to human cells. The specification asserts that SEQ ID NO:4 encodes a polypeptide designated as OrfB, which does not have homology to any presently known proteins. The specification asserts that this protein possesses the ability to form a complex with the protein PilC and to induce either alone or in combination with OrfA the adhesion to human cells (Spec. para. 0066).

The instant invention is not considered to have a specific and/or substantial utility, since the instant specification fails to establish that that the disclosed polynucleotide sequences encodes an amino acid which that mediates adhesion of Neisseria cells to human cells explicitly or implicitly as putatively asserted by the instant specification.

The state of the art at the time of filing teaches that interaction of *Neisseria with human cell is complex and is dependent upon the PilC protein expression.* Pathogenic *Neisseria* express type IV pili (tfp), which have been shown to play a central role in the

interactions of bacteria with their environment. The regulation of piliation constitutes a central element in bacterial life cycle. The PilC proteins are outer membrane-associated proteins that have a key role in tfp biogenesis. In pathogenic *Neisseria*, tfp are responsible for adhesion to human host cells. Pilus retraction is responsible for twitching motility, and has been shown to play a central role in the interactions of pathogenic *Neisseria* with human cells. Furthermore Pilus retraction is associated with the relocalisation of mature pilin subunits along the cytoplasmic membrane. Among the components of the neisserial tfp machinery, the PilC proteins play a crucial but still enigmatic role. They are associated with the outer membrane but can also be recovered from purified pili. PilC-null strains show impairment in pilus expression and are not competent for transformation. However, the mechanism by which the PilC proteins promote piliation remains unknown. It is presumed they act as pilus tip adhesins in *Neisseria gonorrhoeae* and the two *pilC loci* harboured by this species are functionally interchangeable. On the other hand, in *Neisseria meningitidis*, only PilC1 is equivalent to the gonococcal PilC proteins and promotes adhesion. PilC2, which is independently expressed from PilC1, fails to promote adhesion despite identical functions in piliation and transformation competence (see Morand et al The EMBO Journal 23(9): 2009–2017, 2004). Since the specification fails to provide any evidence, which establishes that the amino acid sequences of SEQ ID NO:4 encodes for a polypeptide that mediates adhesion of Neisseria cells to human cells explicitly or implicitly, the invention as claimed herein is not supported by either a specific asserted utility or a well-established utility.

In addition, the scope of invention as claimed encompasses any and all variants of nucleotide sequences encoding polypeptide that mediates adhesion of Neisseria cells to human cells (i.e. any fragment or variant encoded any hybridization product and/or having 5% variation). The variations as claimed encompasses the conserved motifs that may be germane to the adhesion of Neisseria cells to human cells (as claimed). It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a

polypeptide and its tertiary structure is neither well understood nor predictable. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function could be ascribed to the gene product (as asserted).

The instant specification does not comply with 35 U.S.C. 101 and 112 since nebulous expressions "biological activity" and "biological properties" do not contain a sufficiently explicit indication of usefulness of compounds and how to use them. The utility requirements must be met at the time of filing and not after someone else identify a utility that had not been disclosed in the specification. The disclosure is insufficient where experimentation is necessary to determine actual uses, or possible lack of uses, of compounds, as well as how to employ them in a useful manner. For example, it cannot be presumed that a steroid chemical compound is "useful" under 35 U.S.C. 101, or that one skilled in the art will know "how to use" it, simply because compound is closely related only in a structural sense to other steroid compounds known to be useful (In re Kirk and Petrow, 153 USPQ 48 (CCPA 1967)). In instant case the mere association with Orf-A or PilC does not teach one skill in the art how to use the invention as claimed, since the disclosure is insufficient and requires further experimentation necessary to determine actual uses or possible lack of uses of the polypeptide, as well as how to employ them in a useful manner. Furthermore considering the instant specification, it cannot be presumed that the asserted use of SEQ ID NO:4 is useful under 35 USC 101/112 or that one skilled in the art will know "how to use" it, simply because polypeptide is associated with peptides that participates in PilC function. In view of the foregoing, one skilled in the art would not readily attribute the asserted biological activity to the nucleotide sequences that encodes SEQ ID NO:4

Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene product. The only immediate apparent utility for the instant invention would be further scientific characterization of the claimed nucleotide sequences as a putative adhesion protein, that promotes the adhesion of Neisseria cells to any and all types human cells.

Claims 1-9 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth *above*, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to an isolated nucleic acid sequence and/or any variant thereof that encodes a lipoprotein or any fragment thereof that mediates adhesion of Neisseria cells to human cells. The specification asserts that SEQ ID NO:4 encodes a polypeptide designated as OrfB, which does not have homology to any presently known proteins. The specification asserts that this protein possesses the

ability to form a complex with the protein PilC and to induce either alone or in combination with OrfA the adhesion to human cells (Spec. para. 0066). Furthermore the scope of invention as claimed encompasses any variant and/or homolog of SEQ ID NO:4, obtainable from any organism other than Neisseria. Besides the nucleotide sequences that encodes the amino acid sequences of SEQ ID NO:4 derived from *Neisseria gonorrhoeae* the specification as filed fails to disclose any other nucleotide sequence (homolog or any variant thereof) that mediates adhesion of Neisseria cells to human cells, and is structurally and functionally similar to the nucleotide sequences that encodes the SEQ ID NO:4.

Applicant is referred to the guidelines for *Written Description Requirement* published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, besides SEQ ID NO:4 the specification does not provide the structure of any other variant of SEQ ID NO:4. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e conserve motifs or domains). Since the specification fails to disclose any other variant of SEQ ID NO:4 with relevant identifying core characteristics, it is not possible to envision the claimed composition. It is not known what are the other nucleotide sequences that encodes SEQ ID NO:4-like proteins that are capable of eliciting the asserted functional activity (i.e. adhesion of Neisseria to human cells). One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). As stated above the disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. Therefore, the limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art

that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genera. The specification fails to define the minimal structure or consensus core structure that defines the genus comprising a nucleic acid sequence that encodes a lipoprotein that mediates adhesion of Neisseria cells to human cells.

Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the variants of nucleic acid sequences as claimed has been defined only by a statement of function that broadly encompasses "a lipoprotein that mediates adhesion of Neisseria cells to human cells", which conveyed no distinguishing information about the identity of the claimed genetic material, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleotide sequences that encodes SEQ ID NO:4, does not reasonably provide enablement for any variant of nucleotide sequences that encodes SEQ ID NO:4-like protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Since the specification fails to disclose any variant of SEQ ID NO:4 for the reasons as set forth above, it is unclear how one skilled in the art use the invention as claimed. The applicant's disclosure does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation, which requires the identification and characterization of not only SEQ ID NO:4 but also any and all variants of SEQ ID NO:4 like proteins for the role of the encoded protein in the adhesion of Neisseria cells to human cells. At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

sk

SUMESH KAUSHAL
PATENT EXAMINER